Innovative Solution for Skin Diseases: Exploring Nano-Polyherbal Formulations as Promising Therapeutic Agents

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1. ABSTRACT

Herbal medicine - Application of herbal medicine is widespread in different regions of the world. Many people worldwide use various plant-based products for treating skin problems. Herbs are a rich source of active ingredients, can be safer and more cost effective for the treatment of different skin diseases. Herbs, the mixture of chemicals in the whole plant work together to give a better effect (called synergy) than a single active ingredient. Herbal formulation relatively safer, nontoxic, non allergic, less side effect, cost effective and does not show MDR on skin infection so recurrence ultimately reduces. polyherbal formulations focuses on scope and opportunities of polyherbal medicines on local and global level.

Nanotechnology improves the permeation/penetration of the bioactive compounds into deeper layers of the skin, providing a depot effect with sustained drug release and specific cellular and subcellular targeting. Herbal formulation prepared by using nanotechnology will be more effective. Nanogel Nanoemulgel, Nanocarriers are some examples which provide advances in dermatology and systemic treatments. Bacterial skin infections are mild and easily treatable, but some kind of bacterial infections can become very serious and even severe and life threatening. In addition, some bacterial infections can be contagious. This is why prevention at early stage is so important.

With this motto, this project proposal is prepared. It involves phytochemical, pharmacological screening of some herbs and formulate nano polyherbal formulation for skin diseases.

Key words: MDR, recurrence, polyherbal, skin infections, Nanotechnology, dermatology, penetration.

2. INTRODUCTION

Skins anatomy and its types: The skin is the largest organ of the body, accounting for about 15% of the total adult body weight. It performs many vital functions, including protection against external physical, chemical, and biologic assailants, as well as prevention of excess water loss from the body and a role in thermoregulation. The skin is continuous, with the mucous membranes lining the body's surface[1]. The integumentary system is formed by the skin and its derivative structures. The skin is composed of three layers: the epidermis, the dermis, and subcutaneous tissue. The outermost level, the epidermis, consists of a specific constellation of cells known as keratinocytes, which function to synthesize keratin, a long, threadlike protein with a protective role. The middle layer, the dermis, is fundamentally made up of the fibrillar structural protein known as collagen. The dermis lies on the subcutaneous tissue, or panniculus, which contains small lobes of fat cells known as lipocytes. The thickness of these layers varies considerably, depending on the geographic location on the anatomy of the body. The eyelid, for example, has the thinnest layer of the epidermis, measuring less than 0.1 mm, whereas the palms and soles of the feet have the thickest epidermal layer, measuring approximately 1.5 mm. The dermis is thickest on the back, where it is 30–40 times as thick as the overlying epidermis[2]. It represents the next most common extra intestinal complication of inflammatory bowel diseases affecting up to 20% of people.

Skin disorder: Previous studies on populations suggest that around 23-33% have a skin problem. Skin conditions are the most frequent reason for people to consult their general practitioner with a new problem. The quality of life of people with skin diseases such as psoriasis, atopic eczema, and acne can be significantly impaired and such impairments can be greater at times than for life threatening conditions such as cancers. Most common skin diseases are concerned with significant psychosocial morbidity which may go unrecognized without the use of appropriate assessment tools. There were nearly 4,000 deaths due to skin disease in 2005 of which 1,817 were due to malignant melanoma[1]. Skin is the largest organ of the body. Common skin disorders are eczema, psoriasis, generalized pruritus, urticaria, Acne, rosaceous, Bacterial, Viral, Fungal infections, disorders of hairs and nails, skin tumors, leg ulcers, leprosy, genital fungal infections, dermatitis, skin allergy, scabies and swellings etc[2].

The important functions of the skin are as follows:

- Provide a protective barrier against mechanical, thermal, physical injury and hazardous substances.
- Prevent loss of moisture.
- Reduce harmful effects of UV radiation.
- Act as a sensory organ.
- Help to regulate body temperature.
- Act as immune organ to detect infection.
- Production of Vitamin D.
- Protect our bodies from germs.
- Allow us to have the sense of touch[3,28].

While performing all these function skins is affected by various diseases and disorders. The most damaging sequence of disruption to the skin is invasion by pathogenic microorganisms. Apart from these there are various allergic conditions which attack the skin which is the most accessible organ of the body, the one most easily traumatized and therefore frequently subjected to infection. Normal human skin is colonized by large numbers of microorganisms that live harmlessly as commensals on its surface[4]. Skin diseases therefore is a complex subject involving diverse microorganisms that exhibit varying aetiological and pathogenic mechanisms. Fungal diseases of the skin are a common public health problem worldwide. The prevalence of skin fungal diseases is expected to reach 20-25% of the world's population and its incidence continues to rise[5]. Fungal skin diseases constitute an important clinical and public health problem in tropical areas of the world where they are rarely managed[6]. There are many species of fungi that cause skin diseases in man. These are mainly Dermatophytes (Trichophyton species, Epidemophyton sp and Microsporon so), Malassezia furfur and Candida species and less commonly Aspergillus species, Trichothecium roseum, Cladosporium sp and Fusarium sp. the people with skin disorders, the skin barrier does not work as well. The skin has less water retaining properties and moisture is easily lost from the skin causing it to dry out easily. Lot of drugs is being tried for skin diseases, but few have indicated drug resistance, and few have serious side effects. The search for newer source of antibiotics is a global challenge for research institutions, pharmaceutical companies, and academics. Many allopathic drugs used are having side effects such as contact allergy, local irritation, scaling, photosensitivity itching and redness etc. to be costly, having side effects to humans. Also, many drugs are toxic at certain concentration. On the other hand the herbal drugs are safe from side effects

as well as harmful effects. In order to prevent antibiotics resistance of pathogen there is need to discover the new compounds. Medicinal plants have a great potential to cure the different diseases but also as a potential material for maintaining good health. Ayurveda is a traditional system of medicine. The philosophy behind the ayurveda is preventing unnecessary suffering and living a long healthy life[8]. Ayurveda involves the use of natural elements to eliminate the root cause of disease by restoring balance at the same time create a healthy life-style to prevent the recurrence of imbalance[4]. In ayurveda single or multiple herbs are used for the treatment. The ayurveda literature highlighted the concept of poly herbals to achieve a greater therapeutic effect. The active phytochemical constituents of individual plants are insufficient to achieve a desirable therapeutic effect and reduce the toxicity[9].

Needs of Herbal preparation: Application of traditional herbal medicine is widespread in different regions of the world. Many people worldwide use various plant-based products for treating skin problems · These herbs are a rich source of active ingredients can be safer and more cost effective for the treatment of different skin diseases [8].

Nanotechnology: It is one of the key novel drug delivery methods under investigation, with nano-formulations thought to have a wide variety of benefits in comparison with conventional preparations of plant constituents, which include enhanced permeability, solubility, bioavailability, therapeutic activity, stability, improved distribution within tissues and sustained delivery[10 ·]

Literature survey reveals that plants have always been proven as a better source of drugs, when it comes to treatment of skin diseases. Hence, it is an emergence worth to undertake this study to design and develop the polyherbal nano-formulation approaches that have been developed and successfully used as a means to enhance the topical delivery of natural bioactives, including nanoemulsions, liposomes, phytosomes, microspheres, transferosomes, nanogel and also cream, lotion, ointment, gel etc. for the treatment of Acne, Eczema, Psoriasis, Dermatitis, Warts, Sunburn, Impetigo, Pruritus, Urticaria, Skin allergy, Swellings and other infectious skin diseases[11]

3. Literature survey:

Ms. Kashyab Tamboli et.al. (2023): is study was aimed to formulate herbal nanoemulgel containing neem oil extract and aloe-vera gel for the treatment of cutaneous fungal infection against the Candida albicans. Nanoemulsion formulations were prepared by spontaneous emulsification method and characterization of the prepared nanoemulsion formulations were done and optimized NE formulation was incorporated into gel base to obtain nanoemulgel. From the results it can be concluded that nanoemulgel formulation is potential and effective topical drug delivery system for neem oil and aloe-vera gel for the topical treatment of fungal infections[12].

Prakash Vaman Rao Diwan et al. (**2023**): A patent on herbal formulation useful as therapeutic and cosmetic applications for the treatment of general skin disorders[13].

Sudipta Das et.al. (2022): Formulated and evaluated an herbal gel containing Clerodendron infortunatum leaves extract used for certain skin diseases, inflammation, burning sensation. This study reveals that natural remedies are more acceptable in the belief that they are safer with fewer side effects than the systemic ones. These herbal formulations have growing demand in the world market[14].

Saloni Khogta et.al. (2020): Herbal nano- formulation topical delivery Nanogel formulations were prepared by cold method and characterization of the prepared herbal nanogel formulations were done by adding herbal extract incorporated into gel base to obtain nanogel. From the results it can be concluded that nanogel formulation is potential and effective topical drug delivery system for fungal infections.[15]

Fatima reyes-jurado et.al. (2019): Antimicrobial activity of Mexican oregano (*Lippia berlandieri*), thyme (*Thymus vulgaris*), and mustard (*Brassica nigra*) essential oils in gaseous phase. Chemical composition of EOs was analyzed by gas chromatography coupled to mass spectrometry. The minimum inhibitory concentration (MIC) for each EO was determined by the inverted-dish technique. Results showed that the tested EOs displayed significant ($p < 0.05$) antimicrobial effects with MICs in the range of 0.012–1.0 µg/mL of air. Identified compounds in the oils suggest that allyl isothiocyanate (in mustard EO); *p*-cymene, linalool, and thymol (in thyme EO); and *p*-cymene and carvacrol (in oregano EO) were the active compounds with antimicrobial activities. Evaluated microorganisms exhibited different sensitivity to tested EOs in gaseous phase [16].

Ameena Ali et.al (2018): The fundamental study of antimicrobial activity of *Piper betle* extract in commercial toothpastes. In that study, the effects of different solvents (ethanol and water) on the

extraction of the bioactive compounds were investigated. 95% ethanol was found to recover the highest phenolic content of 840 mg GAE/g, followed by 50% ethanol with 460 mg GAE/g and water with the lowest at 200 mg GAE/g. With its high phenolic content, the 95% ethanol extract was blended into 3 existing, commercially available, toothpastes to evaluate its antimicrobial activity. The extract combined with conventional toothpastes, each with different active ingredients, were subjected to four oral bacterial pathogens, *Escherichia coli*, *Staphylococcus aureus, Streptococcus mutans* and *Streptococcus salivarius,* as well as the oral fungal pathogen *Candida albicans, via* agar well diffusion assay. A statistically significant increase in the zone of inhibition after the addition of the *P.betle* extract was observed with all 3 toothpastes in all bacterial and fungal pathogens tested. The greatest increase in ZOI was 24.6% for the bacterial pathogens and 20.3% for the fungal pathogen[17].

Arvind negi et.al. (2018) evaluated a noble herbal gel formulation containing extract from the leaves Eupaterium adenophorum for its topical anti-inflammatory activity against carrageenan induced oedema. This study reveals that such gel possesses significant topical anti-inflammatory properties, supporting their traditional use for the treatment[18]

Shasikala et.al. (2018): Identified compounds by GC-MS which is useful antimicrobial activities against Staphylococcus aureus and Enterococcus faecalis and also against a fungi Aspergillus niger. The ethanolic extract was subjected to Gas chromatography-mass spectrometry (GC-MS) analysis for identification of compounds present in fruit sample. The identified compounds were then screened for anti-inflammatory activity by molecular docking against the Cyclooxygenase-2 inhibitors. Also, Density Functional Theory (DFT) & Absorption Distribution Metabolism Excretion and Toxicity (ADMET) studies were carried out to assess the quantum-chemical parameters and pharmacokinetics behaviour respectively. The ethanolic fruit extract of A. indicum showed antimicrobial activity against S. aureus, E. faecalis and Aspergillus niger[19]

Ramanarayana Reddy RV et.al (**2014**): Evaluation of diuretic and anti-inflammatory antimicrobial property of ethanolic extract of solanum surattense in experimental animal models.**P**harmacological and phytochemical traits Studies and research conducted have revealed that the plant's medicinal benefit includes anti-inflammatory, bronchodilator, anti-microbial wound-healing, anti-cancer, and insecticidal properties[20]

Y,m, charde et. al (2014): Formulated and evaluated a herbal formulation for the treatment of acne. The present research work deals with formulation of herbal gel with ethanolic extracts of Neem (leaves), Nutmeg (fruit) and Black pepper (fruit) and evaluated for various physicochemical properties and antimicrobial activity. From evaluation it is concluded that this is an effective polyherbal formulation for the treatment of acne [21].

Allah Nawas et. al (2014): Formulated a topical polyherbal formulation Dermidoc cream consisting of natural ingredients that have been clinically proved for its anti-itching and anti-inflammatory activity and has been advocated to treat skin ailments especially dermatitis. Dermidoc cream consist of Cleome brachycarpa, Calendula officinalis, Psoralen carylifolia and Rheum emodi wall. From evaluation it is concluded that Dermidoc cream has shown efficacy in mild to moderate cases on applying locally to the affected parts [22].

Kavitha A N et.al (2013): Designed, formulated and evaluated a polyherbal ointment comprising of methanolic extract of the leaves of Tectona grandis, Ficus religiosa, **Caesalpinia** etc. This study revealed that the polyherbal ointment may be used as a potential herbal formulation for wound healing[23].

Prasana A. Datar. (2013): Formulated and evaluated polyherbal gel prepared using carbopol 934 for treating skin diseases in comparison with ointment using emulsifying ointment. This study deals with topical drug delivery system composed of polyherbal including Neem, Tulsi, Aloe and fenugreek which are having antifungal and antibacterial activity in the form of gel and were 6 evaluated for various physicochemical parameters like pH, viscosity, spreadability, skin irritations test and microbial evaluations. Such study reveals that gels are free from irritation and have better antimicrobial activity and this gel can be used for treating skin diseases[24].

P.H. Rajasree et.al. (2012) Formulated and evaluated antiseptic polyherbal ointment. The ointment were formulated using methanolic extract of Azardirachta indica, chromolaena odorata, mimosa pudica, samadera indica and evaluated for its physicochemical propertiey, antibacterial and antioxidant activity. Overall result of this study reveals that this is an effective polyherbal antiseptic oinmeant[25]

Smita Jain and u.k.patil (2011): Formulated a polyherbal cream with wound healing activity. Formulation was designed by using ethanolic extract of Argemone Mexicana, Cassia Tora, Evolvulus Alsinoids, Ocimum Centum, Curcumas Sativus by phase inversion emulsification techniques. After evaluation the formulated herbal cream is most effective and safer usage in wound repair process[26].

Samadhan Dahikar et.al. (2010): Evaluation of antibacterial potential of Trikatu churna and its ingredients: An in vitro study. Trikatu churna were prepared and antibacterial activities were tested by disc diffusion method against enteric bacterial pathogens such as Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Proteus vulgaris, Staphylococcus epidermidis, Salmonella typhi, Salmonella typhimurium and Enterobacter aerogenes. The extracts of Piper longum, Piper nigrum and Zingiber officinale were found antibacterial to all bacterial pathogen tested. Trikatu churna exhibited potent antibacterial activity; this might be due to the multifunctional effect of all the three plant ingredients of Trikatu churna. Antibacterial activity of Trikatu churna and its ingredients was carried out in attempt to support the use of Trikatu churna for the treatment of enteric bacterial infections [26].

Anand kumar et.al. (2001): Developed a herbal formulations which has anti-inflammatory and immuomodulatory properties and is a chelating agent for various toxins in the blood. And has been advocated to treat various skin disorders such as chronic lichens planus, psoriasis, chronic lichen simplex, chronic eczema and various allergies lead to dermatitis[27]

Literature survey reveals that many medicinal plants prove to be an excellent topical antimicrobial potential, helps to prevent infections of bacterial, fungal or any microbe.

4. EXPECTED OUTCOME OF RESEARCH

The given research explores the selected medicinal plants for its pharmacological activities. It is novel approach to formulate polyherbal preparation.

Polyherbal nano formulations have gained considerable attention in recent years due to their potential therapeutic benefits for various skin diseases. These formulations combine multiple herbal extracts or compounds with nanotechnology to enhance their bioavailability, stability, and targeted delivery. While specific outcomes may vary depending on the formulation and the skin disease being treated, here are some expected outcomes of polyherbal nano formulations for skin diseases.

Enhanced skin penetration: Nano-sized particles in the formulation can penetrate the skin more effectively, allowing the active ingredients to reach the target site and exert their therapeutic effects. This improved penetration can be particularly beneficial for skin diseases that involve deep layers of the skin.

Increased bioavailability: Nano formulations can improve the solubility and stability of active compounds, leading to increased bioavailability and effectiveness. This means that a smaller dose of the formulation may be needed to achieve the desired therapeutic effect compared to traditional formulations.

Controlled release: Nanotechnology enables the controlled release of active ingredients, prolonging their presence at the site of action and ensuring a sustained therapeutic effect. This can be advantageous for chronic skin conditions that require long-term treatment.

Anti-inflammatory effects: Anti-inflammatory effects seen in many skin diseases, such as eczema, psoriasis and acne.

5. Rationales of Research Works:

1. **Skin Anatomy**: One of the main functions of the skin is protection. It protects the body from external factors such as bacteria, chemicals, and temperature. The skin contains secretions that can kill bacteria and the pigment melanin provides a chemical pigment defense against ultraviolet light that can damage skin cells.
2. **Skin diseases**: The Global Burden of Disease project has shown that skin diseases continue to be the 4th leading cause of nonfatal disease burden world-wide. However, research efforts and funding do not match with the relative disability of skin diseases. International and national efforts, such as the WHO List of Essential Medicines, are critical towards reducing the socioeconomic burden of skin diseases and increasing access to care. Recent innovations such as teledermatology, point-of-care diagnostic tools, and task-shifting help to provide dermatological care to underserved regions in a cost-effective manner. Also cost-effective product from natural origin synthetic product is too costly.
3. **Herbal medicines**: Herbs the mixture of chemicals in the whole plant work together to give a better effect (called synergy) than a single active ingredient. Herbal formulation relatively safe, nontoxic and does not form MDR on skin infection so recurrence ultimately reduces. polyherbal formulations focuses on scope and opportunities of polyherbal medicines on local and global level.
4. **Importance of Nanotechnology**: Nanotechnology improves the permeation/penetration of the bioactive compounds into deeper layers of the skin, providing a depot effect with sustained drug release and specific cellular and subcellular targeting. Nanogel Nanoemulgel, Nanocarriers are some examples which provide advances in dermatology and systemic treatments. bacterial skin infections are mild and easily treatable, some can become very serious and even life threatening. In addition, some bacterial infections can be spread to others. This is why prevention is so important.

6. Aim objective and Rational of research work:

Aim: Innovative Solution for Skin Diseases: Exploring Nano-Polyherbal Formulations as Promising Therapeutic Agents.

Objective and Rational of research work:

The objective is to find out and confirm the phytoconstituents in the extracts of plants and develop polyherbal formulations which can be topically used to treat skin disease caused by various microorganisms (fungus and bacteria).

- **Specific objectives include:**

1. Selection and authentication of lead plants possessing desired activity.
2. Extraction/ macerations selected plant part(s).
3. Phytochemical screening
4. Nanoparticulate plant extract(s).
5. Development of nano- formulations using plant extract(s).
6. Evaluation parameters of formulation**.**
7. Report writing and publication.
8. Thesis submission

7. Materials and Methods of Research:

Materials: Plant materials will be collected/ procurement, authenticates and extracted.

Methods:

1. **Collection and authentication of plant material.**

   The plant will be collected, authenticated, cleaned, dried and powdered for further process.

2. **Preliminary Phytochemical Investigation.**

   A. Extraction: The plant materials will be subjected for extraction with different solvents (Non-polar to Polar).

   B. Preliminary phytochemical investigation: Preliminary phytochemical investigation of extract is carried out by qualitative chemical test.

3. **Acute toxicity and irritation study.**

   For the determination of safe dose of polyherbal formulation will be subjected for the acute toxicity.

4. Formulation of polyherbal formulation.

5. Evaluation for various physicochemical parameters.

- pH
- Viscosity
- Spreadability
- Extrudability
- Skin irritancy study
- In-vitro diffusion study
- Stability studies[25].

6. Pharmacological screening of polyherbal formulations.

The polyherbal formulations will be subjected for study of antibacterial, antifungal and anti-inflammatory activity using screening model

8. Proposed work plan

Present study is designed in such a way that it will come to a conclusive outcome within 03 years from the date of Allocation. The plan & duration of work is as follows.

Sr. No.	Work to be completed	Duration
1	Review of Literature	8 month
2	Collection and authentication of procurements plant materials	2 month
3	Extraction, Preliminary phytochemical analysis.	6 month
4	Development of polyherbal formulation(s).	6 month
5	Physical evaluation of formulation(s).	2 month
6	Acute toxicity irritation study	2 month
7	Pharmacological screening of formulation	6 month
8	Data interpretation and thesis writing	4 month

9. References:

1. Kanitakis, J. (2006): Anatomy, histology and immunohistochemistry of normal human skin. European Journal of Dermatology, 12(4), 390–401.
2. James, W.D., Berger, T.G., & Elston, D.M. (2006). Andrews' diseases of the skin: Clinical dermatology (10th ed.). Philadelphia: Elsevier suanders.
3. Kohen R. Skin antioxidants (1999): Their role in aging and in oxidative stress- New approaches for their evaluation. Biomedicine and Pharmacotherapy, 181-192.
4. Ro BI, Dawson TL. (2005): The role of sebaceous gland activity and scalp microoral metabolism in the etiology of seborrheic dermatitis and dandruff. J Investigative Dermatol SP. 2005; 10(3): 194-7
5. Ndubuisi Nwachukwu. (2021): Dermatology, An Illustrated Colour Text. 3rd ed. Edinburgh: Churchill Livingstone; 2002. Fungal and Yeast Involvement in Skin Diseases Microbiology and Pathology Fungal and Yeast Involvement in Skin Diseases. Global Journal of Medical Research 16(3):43-47
6. Latha PS, Kannabiran K. (2006): Antimicrobial activity and phytochemicals of Solanum trilobatum Linn. African Journal of Biotechnology. 2006;5: 2402-2404.
7. Chah KF, Eze CA, Emuelosi CE, Esimone CO. (2006) Antibacterial and wound healing properties of methanolic extracts of some Nigerian medicinal plants. Journal of Ethnopharmacology. 2006;104: 164-167.
8. Subramani Parasuraman, Gan Siaw Thing, and Sokkalingam Arumugam Dhanaraj. (2014)P: Polyherbal formulation: Concept of ayurveda,Pharmacogn Rev. 2014 Jul-Dec; 8(16): 73–80.(intro ayurveda)
9. Farnsworth N.R, Bingel A.S, Soejarta D.D and Eno Z. (1985): Medicinal plants in therapy, Bulletin-WHO, 63(6), 965-981.
10. Sudipta Das1,2*,Pallab K. Haldar2, Goutam Pramanik (2011): Formulation And Evaluation Of Herbalgel Containing Clerodendron Infortunatum Leaves Extract, International Journal Of Pharmtech Researchcoden (USA): IJPRIF ISSN : 0974-4304,Vol. 3, No.1, Pp 140-143, Jan-Mar 2011.
11. Arnabaditya M, Chandan D, Sujit D, Durga CS. (2010): Physico-Chemical and antimicrobial study of polyherbal formulation Int J Compre Pharm 2010;1(4):
12. Ms. Kashyab Tamboli (2023): Formulation, Development and Evaluation of Herbal Antifungal

Nanoemulgel Containing Neem Seed Oil, Tulsi Oil and Aloe-Vera Gel. International Journal of Advanced Research in Science, Communication and Technology (IJARSCT);3(1) 2581-9429

13. Prakash Vaman Rao Diwan, Bhami Dipali Subrahmanya Sitaraman, Sistla Ramkrishna, Khandapuram Vijaya Raghvan.(2023) A Patent on Herbal Formulations Useful as Atherapeutic And Coemetic Applications For The Treatment Of General Skin Disorders.
14. Saloni Khogta (2020): Herbal nano-formulations for topical delivery. Journal of herbal medicine, 2020:20
15. Fatima Reyes-Jurado (2019): Antimicrobial activity of Mexican oregano (*Lippia berlandieri*), thyme (*Thymus vulgaris*), and mustard (*Brassica nigra*) essential oils in gaseous phase. *Industrial Crops and Products (131): 90-95*
16. Ameena Ali (2018): The fundamental study of antimicrobial activity of *Piper betle* extract in commercial toothpastes. The *Journal of Herbal Medicine* 2018 (14): 29-34
17. Arvind Negi, Nimisha Sharma, Mamla F Singh. (2018): Formulation And Evaluation Of Herbal Antiinflammatory Gel Containing Eupaterium Leaves Extract, Journal Of Pha Rmacognosy And Phytochemistry, ISSN 278-4138, IC. 11
18. R.P.Shasikala (2018); Identification of biological activities of *Abutilon indicum* fruit by *in silico* and *in vitro* approach; Karbala International Journal of Modern Science 4(3), 287-296
19. Ramanarayana Reddy RV, Uma maheshwara Rao (2014): Evaluation of diuretic and anti-inflammatory property antimicrobial of etholic extract of solanum surattense in experimental animal models. Int J Pharm Pharm Sci, 2014; 6(1):387–9.
20. Y.M. Charde, P.H. Sharma, N.G. Choudhary and J.G. Avari (2014): Development And Evaluation of Herbal Formulation For The Treatment Of Acne, IJPSR, 2014; Vol. 5(6): 2250-2260.
21. Allah Nawaz, Zeeshan Ahmed Sheikh, Kamran Alam, Rabia Bashir &Khan Usmanghani (2014): Clinical Efficacy of Polyherbal Formulation Dermidoc Cream For Dermatitis, International Journal of Humanities, Arts, Medicine And Sciences (Best: Ijhams) Issn 2348-0521 Vol. 2, Issue 10, 2014;75-80.
22. Kavitha AN1, Deepthi V1 And Naira Nayeem2* (2013): Design, Formulation and Evaluation of A Polyherbal Ointment For Its Wound Healing Activity, Pharmacophore 2013, Vol. 4 (5), 175-180.
23. Prasanna A Datar (2013): Formulation and Evaluation f The Polyherbal Gel Prepared Using Carbopol 934 For Treating Skin Diseases In Comparison With Ointment Using Emulsifying

Ointment.Research And A Reviews: Journal Of Pharmaceutics And Nanotechnology.

24. P.H.Rajasree Vidya Vishwanad. (2012): Merin Cherian1, Jincy Eldhose1 And Ranjith Singh2, Formulation And Evaluation Of Antiseptic Polyherbal Ointment, International Journal Of Pharmacy &Life Sciences, 3(10): Oct., 2012] ISSN: 0976-7126.
25. Smita Jain And U.K. Patil, (2011): Formulation and Characterization Of Polyherbal Cream With Wound Healing Activity. Pharmacologyonline 3:1470-1477. (2011)
26. Samadhan Dahikar (2010): Evaluation of antibacterial potential of Trikatu churna and its ingredients: An in vitro study. International Journal of Phytomedicine 2:412-417
27. Anand Kumar, (2001): A Herbal Formulation In The Treatment Of Different Types Of Dermatitis, [The Indian Practitioner (2001): (54), 8, 571-575
28. Sandya D, Akbar A, Mahesh G, Bhaskar G, Yogesh M. (2010): Comparative evaluation of poly herbal formulation for anti-inflmmatory and analgesic activity in rats and mice. Der Pharmacia, 2010;2(1)285-290.

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